JAMES MADISON UNIVERSITY

SEMINAR
Friday, September 25

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Diversity and Vulnerability in Bacterial ATP Synthesis

Abstract: ATP is the universal energy currency of known life, and most of it is made by ATP synthases in the process of oxidative phosphorylation. F_1F_o ATP synthase catalyzes the final step of this process in bacteria, mitochondria, and chloroplasts by using an electrochemical gradient of H^+ to drive a rotary mechanism that condenses ADP and phosphate into ATP. While much is understood about this mechanism, we do not have a complete understanding of how H^+ moves through the membrane-embedded F_o motor during ATP synthesis or during ATP-powered H^+ pumping. Using cryo-electron microscopy and extensive mutagenesis of enzymes from *E. coli* and *Pseudomonas aeruginosa* (PA), we found unexpected differences in the H^+ channels and revealed new roles for amino acid residues in the rotor-stator interface. Understanding the distinct features of these enzymes reveal vulnerabilities that can be exploited for antibiotic development. PA and *Acinetobacter baumannii* are Gram-negative bacteria identified as particular threats to public health, and both require ATP synthase for survival. We have synthesized a library of ~200 compounds targeting the rotor-stator interface of ATP synthase, some of which show promising antibacterial activity.

Meet the Speaker **2:00 pm, PCB 3144**
Seminar **3:30 pm, King 159**